

Path integrals for stiff polymers applied to membrane physics

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(Dated: 11 April 2007)

Path integrals similar to those describing stiff polymers arise in the Helfrich model for membranes. We show how these types of path integrals can be evaluated and apply our results to study the thermodynamics of a minority stripe phase in a bulk membrane. The fluctuation induced contribution to the line tension between the stripe and the bulk phase is computed, as well as the effective interaction between the two phases in the tensionless case where the two phases have differing bending rigidities.

I. INTRODUCTION

Recently there has been much interest in the effective interactions between components of membranes of different composition. These effective interactions can be direct basic interactions such as electrostatic and van der Waals forces. However the fact that the membrane fluctuates also leads to effective interactions which are due to how the different components, or inclusions, alter the membrane fluctuations. Coarse grained models, based on the Helfrich model [1, 2], of multicomponent membrane describes the membrane in terms local mechanical properties, for instance the bending rigidity κ_b , the Gaussian rigidity κ_g or the spontaneous curvature [10, 11, 12, 13, 14, 15, 16]. The effective, fluctuation mediated, interaction between regions of differing rigidity can be computed using a cumulant expansion giving the effective pair-wise component of the interaction between two regions. This term is of order $\delta\kappa_{b/g}^2$ and is the analogue of the pair-wise component of van der Waals forces. However when $|\delta\kappa_{b/g}|$ is large then this two-body, or dilute, approximation will break down and a full N -body calculation is needed. We should expect the dilute approximation to break down reasonably frequently as experimentally measured values of κ_b for commonly occurring lipid types vary from 3 to $30k_B T$.

In this paper we show how the full N -body calculation for a system with spatially varying rigidity and elasticity, can be carried out for stripe geometries of the type shown in Figure 1. Within this geometry we can compute the contribution to the line tension between the two phases due to membrane fluctuations. This can be seen as a renormalization of the line tension already present due to basic interactions such as van der Waals, electrostatic and steric forces. In addition, in some cases, we can evaluate the effective interaction between the two interfaces as a function of their separation l .

They key point in our calculation is that we convert the usual functional integral into a path integral where the direction in which the physical parameters change is treated like a fictitious time variable within the path integral formalism. The authors have already applied this approach to electrostatic problems where it has proved to be efficient for carrying out computations for films [7], interfaces [8] and in cylindrical geometries such as lipid-tubules [9].

The paper is organized as follows. In section II we describe the model and show how it can be analyzed using path integrals which are mathematically identical to those arising for stiff polymers. In section III we present the results of our computations. We start with an analysis of bulk homogeneous membranes and show how some standard results can be recovered using our path integral formalism and then how the method can be applied to a striped membrane system. The formalism is then used to compute the membrane fluctuation-induced contribution to the line tension between two phases. In section IV the fluctuation-induced Casimir force in a striped system is calculated for typical physical situations. In section V we conclude with a discussion of our results. The generalized Pauli-van Vleck formula used to evaluate the path integrals is described in detail in Appendix A. Some aspects of this approach have been previously described in the literature [4, 5, 6], however our approach is slightly different and self-contained. Hence for the sake of completeness (and because the results seem to be relatively unknown) we include this detailed description of the approach.

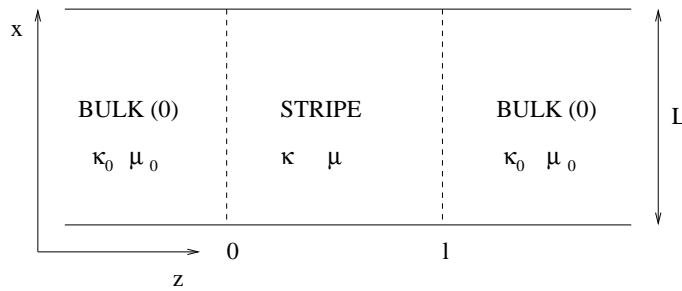


FIG. 1: Schematic diagram of striped membrane configuration with mechanical parameters (rigidity and elasticity indicated).

II. THE MODEL

In the Monge gauge the Helfrich model for a membrane whose height fluctuations are denoted by h is given by

$$H = \frac{1}{2} \int_{A_p} d^2 \mathbf{x} \left[\kappa (\nabla^2 h)^2 + \mu (\nabla h)^2 \right]. \quad (1)$$

In this model we have neglected the Gaussian rigidity κ_g and so for ease of notation we denote the bending rigidity simply by κ . In this form of the Helfrich model there is no spontaneous curvature and it is implicitly assumed that the fluctuations of h are small. The term μ can be interpreted as a local elastic or surface energy. When μ is constant it can be interpreted as a surface tension. The integral in $\mathbf{x} = (z, y)$ in Equation (1) is over the projected area of the membrane A_p . The physical area of the membrane is larger than A_p due to fluctuations and we denote it by $A = A_p + \Delta A$, where ΔA is the excess area due to fluctuations. In the limit of small height fluctuations (i.e. to quadratic order in h) the excess area is given by

$$\Delta A = \frac{1}{2} \int_{A_p} d^2 \mathbf{x} (\nabla h)^2. \quad (2)$$

The canonical partition function can be written as a functional integral over the height field h

$$Z = \int d[h] \exp(-\beta H), \quad (3)$$

where $\beta = 1/k_B T$, T is the canonical temperature and k_B Boltzmann's constant.

If the mechanical parameters κ and μ only vary with the coordinate z then we can express h in terms of its Fourier decomposition in the direction y writing

$$h(z, y) = \frac{1}{\sqrt{L}} \sum_k \tilde{h}(z, k) \exp(iky). \quad (4)$$

We have imposed periodic boundary conditions in the y direction and thus have $k = 2\pi n/L$, where L is the width of the system and n is an integer. Note that we are assuming that the interfaces between differing phases are straight and thus lie at constant values of z . This is a realistic assumption if the bare (in the absence of height fluctuations) line tension γ_0 is positive and large. We will in fact see that the renormalization of the line tension γ between phases due to the height fluctuations is positive and thus this assumption remains valid (and is in fact reinforced) by height fluctuations.

In the limit of large L the sum over modes can be written as

$$\sum_k \rightarrow L \int \frac{dk}{2\pi}. \quad (5)$$

We now find that the Hamiltonian decomposes as

$$H = \sum_k H_k, \quad (6)$$

where

$$H_k = \frac{1}{2} \int dz \kappa(z) \left(\frac{\partial^2 \tilde{h}(z, -k)}{\partial z^2} \frac{\partial^2 \tilde{h}(z, k)}{\partial z^2} \right) + (2\kappa(z)k^2 + \mu(z)) \left(\frac{\partial \tilde{h}(z, -k)}{\partial z} \frac{\partial \tilde{h}(z, k)}{\partial z} \right) + (\mu(z)k^2 + \kappa(z)) \tilde{h}(z, k) \tilde{h}(z, -k). \quad (7)$$

The field h is real and so we have the relation $\bar{\tilde{h}}(z, k) = \tilde{h}(z, -k)$. The full functional integral for the partition function Z can then be written as

$$Z = \prod_{k \geq 0} \Theta_k, \quad (8)$$

where

$$\Theta_k = \int d[X] \exp \left(-\frac{1}{2} \int_0^l dt \left[a_2(k, t) \left(\frac{d^2 X}{dt^2} \right)^2 + a_1(k, t) \left(\frac{dX}{dt} \right)^2 + a_0(k, t)^2 X_t^2 \right] \right). \quad (9)$$

In the above, the coefficients are given by

$$\begin{aligned} a_2(k, t) &= \beta \kappa(t) \\ a_1(k, t) &= \beta (2\kappa(t)k^2 + \mu(t)) \\ a_0(k, t) &= \beta (\mu(t)k^2 + \kappa(t)), \end{aligned} \quad (10)$$

and l is the length of the system (in the z direction). The above path integral is that arising in an elastic model of a semi-flexible polymer [3] (in one dimension) where $\kappa = a_2/\beta$ is the rigidity of the polymer, the term proportional to a_1 represents the elastic energy and the term proportional to a_0 represents an external harmonic potential. In this model the length of the polymer is not fixed, in contrast to the worm-like chain model where the magnitude of the tangent vector is fixed. The method of evaluation of the above type of path integral is given in Appendix A and we find that it takes the form

$$K(\mathbf{X}, \mathbf{Y}; t) = (2\pi)^{-\frac{N}{2}} [\det(B(t))]^{\frac{1}{2}} \exp \left(-\frac{1}{2} \mathbf{X}^T A_I(t) \mathbf{X} - \frac{1}{2} \mathbf{Y}^T A_F(t) \mathbf{Y} + \mathbf{X}^T B(t) \mathbf{Y} \right), \quad (11)$$

where the initial condition vector is $\mathbf{X} = (X, U)$ with $X = X(0)$ and $U = dX/ds|_{s=0}$, and the final condition vector is $\mathbf{Y} = (Y, V)$ with $Y = X(t)$ and $V = dX/ds|_{s=t}$. When the coefficients a_k are independent of t the classical action can be written as a combination of surface terms (using the equation of motion) as

$$S_{cl}(\mathbf{X}, \mathbf{Y}) = \frac{1}{2} \left(a_2 \left[\frac{dX}{ds} \frac{d^2 X}{ds^2} \right]_0^t - a_2 \left[X \frac{d^3 X}{ds^3} \right]_0^t + a_1 \left[X \frac{dX}{ds} \right]_0^t \right). \quad (12)$$

The above expression is in general rather complicated but can be used to determine the matrices A_F , A_I and B . Also, when the coefficients are independent of time, the time reversed trajectories have the same weight as the original trajectories. Thus the path integral going from (X, U) to (Y, V) in time t has the same value of the path integral going from $(Y, -V)$ to $(X, -U)$ in time t . Mathematically this means that

$$A_F = S A_I S, \quad (13)$$

and

$$B^T = S B S, \quad (14)$$

where

$$S = \begin{pmatrix} 1 & 0 \\ 0 & -1 \end{pmatrix}. \quad (15)$$

In the limit of large t the propagator K should factorize, as it is dominated by the lowest eigenfunction, and so we should find that $B(t) \rightarrow 0$ as $t \rightarrow \infty$. This can be verified by explicit calculation in the cases considered here.

III. CALCULATIONS FOR BULK AND STRIPED SYSTEMS

To start with we will show how the path integral formalism introduced here reproduces some standard results concerning bulk systems. We consider a bulk system of projected length l and projected width L ; we thus have a projected area $A_p = Ll$. Periodic boundary conditions are imposed in both directions z and y . The free energy is given by

$$F = -k_B T \sum_k \ln(\Theta_k), \quad (16)$$

where

$$\Theta_k = \int d\mathbf{X} K_k(\mathbf{X}, \mathbf{X}, l). \quad (17)$$

Using Equation (A17) and the notation developed in the appendix we find

$$\Theta_k = \det(B(k, l))^{\frac{1}{2}} \det(A_I(k, l) + A_F(k, l) - 2B(k, l))^{-\frac{1}{2}}. \quad (18)$$

The classical equation of motion in this case has solutions

$$X(t) = a \cosh(pt) + b \sinh(pt) + c \cosh(qt) + d \sinh(qt), \quad (19)$$

where

$$p = k, \quad (20)$$

and

$$q = (k^2 + m^2)^{\frac{1}{2}}, \quad (21)$$

where we have defined

$$m^2 = \frac{\mu}{\kappa}, \quad (22)$$

and so m is an inverse length scale. The expressions for A_F , A_I and B can be computed using computer algebra but they simplify in the (thermodynamic) limit $l \rightarrow \infty$. We define

$$A_{I/F}^* = \lim_{l \rightarrow \infty} A_{I/F}, \quad (23)$$

and find that

$$A_I^* = \beta \kappa \begin{pmatrix} pq(p+q) & pq \\ pq & (p+q) \end{pmatrix}. \quad (24)$$

We also find that for large l $B(l) \rightarrow 0$, and

$$\det(B(l)) \approx pq(p+q)^2 \exp(-(p+q)l). \quad (25)$$

The extensive part of the bulk free energy is thus

$$\frac{F}{A_p} = \frac{k_B T}{2\pi} \int_{\frac{\pi}{L}}^{\frac{\pi}{a}} dk \left[k + (k^2 + m^2)^{\frac{1}{2}} \right], \quad (26)$$

where we have introduced the ultra-violet cut-off length scale a which corresponds to the lipid size. The infra-red cut-off scale (where needed) is given by L (the lateral size of the system). The excess area of the system is given by

$$\Delta A = \frac{\partial F}{\partial \mu}, \quad (27)$$

and in the tensionless limit where $\mu = 0$ we find the well known result

$$\frac{\Delta A}{A_p} = \frac{k_B T}{4\pi \kappa} \ln \left(\frac{L}{a} \right). \quad (28)$$

In the case where $\mu \neq 0$ we find that

$$\frac{\Delta A}{A_p} = \frac{k_B T}{4\pi\kappa} \sinh^{-1} \left(\frac{\pi}{am} \right). \quad (29)$$

This gives

$$\frac{\Delta A}{A_p} \approx \frac{k_B T}{4\pi\kappa} \ln \left(\frac{2\pi}{am} \right), \quad (30)$$

when $a \ll 1/m$.

For a striped geometry where the length of the bulk phase is l_0 , and large and that of the minority phase is l we find that for this composite striped (hence the superscript s in what follow) system we have, as $l_0 \rightarrow \infty$,

$$\begin{aligned} \Theta_k^{(s)}(l, l_0) &= \int d\mathbf{X} d\mathbf{Y} K_k(\mathbf{X}, \mathbf{Y}, l) K_k^{(0)}(\mathbf{X}, \mathbf{Y}, l_0) \\ &= \left[\det(B^{(0)}(l_0)) \right]^{\frac{1}{2}} \left[\det(B(l)) \right]^{\frac{1}{2}} \left[\det \left(A_F^{(0)*} + A_I(l) \right) \right]^{-\frac{1}{2}} \\ &\quad \left[\det \left(A_I^{(0)*} + A_F(l) - B^T(l) (A_F^{(0)*} + A_I(l))^{-1} B(l) \right) \right]^{-\frac{1}{2}}, \end{aligned} \quad (31)$$

where the superscript (0) refers to the bulk phase and the absence of this superscript refers to the minority phase. In the limit $l \rightarrow \infty$ the above expression simplifies giving

$$\Theta_k^{(s)}(l, l_0) \approx \left[\det(B^{(0)}(l_0)) \right]^{\frac{1}{2}} \left[\det(B(l)) \right]^{\frac{1}{2}} \left[\det(A_I^{(0)*} + A_F^*) \right]^{-1}, \quad (32)$$

where we have used Equation (13). In order to compute the free energy cost of the interface between the two phases we subtract the separate bulk free energies for large systems of size l_0 , corresponding to the bulk, and of size l , corresponding to the minority phase, from that of a large striped system composed of length l_0 of the bulk phase and l of the minority phase. This free-energy difference is

$$\Delta F = -k_B T \sum_k \ln \left(\frac{\Theta_k^{(s)}(l, l_0)}{\Theta_k^{(0)}(l_0) \Theta_k(l)} \right), \quad (33)$$

which gives

$$\Delta F = -\frac{k_B T}{2} \sum_k \ln \left(\frac{\det(A_I^{(0)*} + A_F^{(0)*}) \det(A_I^* + A_F^*)}{\det(A_I^{(0)*} + A_F^*)^2} \right). \quad (34)$$

The above expression is in general quite complicated but when κ and κ_0 are non-zero, then at large k the eigenvalues q (given by Equation (21)) in the stripe phase becomes asymptotically equal to q_0 , the corresponding eigenvalue in the bulk phase. We thus find that the sum in Equation (34) is ultra-violet divergent and is dominated by the term

$$\Delta F = \frac{L k_B T}{a} \ln \left(\frac{1 - \Delta^2/4}{1 - \Delta^2} \right), \quad (35)$$

where

$$\Delta = \frac{\kappa - \kappa_0}{\kappa + \kappa_0}. \quad (36)$$

We may interpret this result as the existence of a height fluctuation induced line tension γ_{hf} between the two phases (note the factor of a half as there are two interfaces) given by

$$\gamma_{hf} = \frac{k_B T}{2a} \ln \left(\frac{1 - \Delta^2/4}{1 - \Delta^2} \right). \quad (37)$$

Thus the dominant contribution to the fluctuation induced line tension between the two phases comes from the mismatch in their bending rigidities. We also remark that it does not depend on m and is only dependent on κ and κ_0

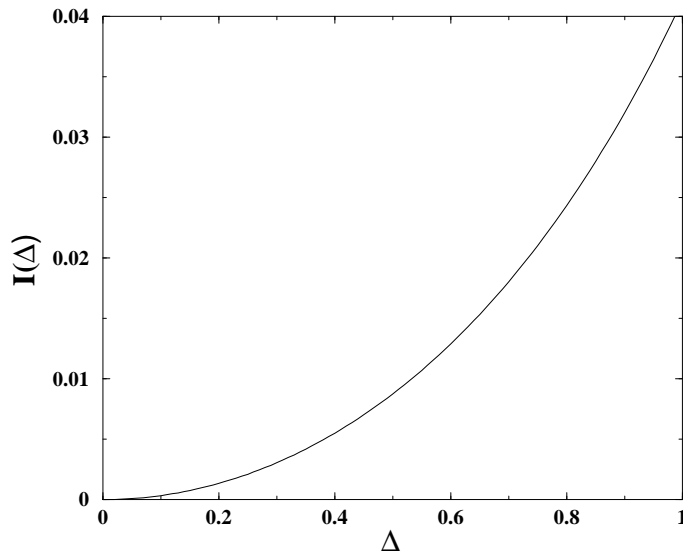


FIG. 2: The function $I(\Delta)$ defined in Equation (38), where $\Delta = (\kappa - \kappa_0)/(\kappa + \kappa_0)$. Note that $I(\Delta) = I(-\Delta)$.

through Δ^2 , which is a symmetric function of the two rigidities. As an example the fluctuation induced line tension between two phases whose rigidity differs by a factor of 10 has an energy of about $0.5 k_B T$ per lipid at the interface.

The correction terms to γ_{hf} are UV convergent and, after some manipulation, γ can be expressed as a power series in ma/π as

$$\gamma_{hf} = \frac{k_B T}{a} \left[\frac{1}{2} \ln \left(\frac{1 - \Delta^2/4}{1 - \Delta^2} \right) + \frac{ma}{\pi} I(\Delta) - \frac{1}{128} \frac{\Delta^2}{(1 - \Delta^2/4)} \left(\frac{1}{3} \left(\frac{ma}{\pi} \right)^4 - \frac{1}{5} \left(\frac{ma}{\pi} \right)^6 \right) \right]. \quad (38)$$

$I(\Delta)$ is shown in Figure 2 for $\Delta > 0$ and is a non-negative function of Δ with $I(0) = 0$ and $I(\Delta) = I(-\Delta)$. From Figure 2 we see that $I(\Delta)$ has a maximum value $I(\infty) \sim 0.04$. For $\mu = 10^{-2} N/m$, $\kappa = 25 k_B T \sim 10^{-19} J$ and $a = 10^{-9} m$, we find $ma = \sqrt{(\mu/\kappa)} a \sim 0.32$ and so $ma/\pi \sim 0.1$. The correction to the leading term due to non-zero μ is thus expected to be certainly less than $O(1\%)$.

IV. APPLICATIONS

In this section we discuss the application of the theory developed above to two cases in the system with a stripe as shown in Figure 1. These cases are distinguished by the values of the masses in the two regions, $m_0 = \sqrt{(\mu_0/\kappa_0)}$, $m = \sqrt{(\mu/\kappa)}$, which control the relationship of the surface to bending energies. In general, the boundary conditions satisfied by the system will vary and will determine the precise way in which our formalism is applied and the form taken by the relevant Helfrich action. We consider two cases that might be thought of as extreme situations and are chosen to show how the results are markedly different depending on the exact situation. We concentrate on computing the Casimir force across the stripe which can be interpreted as a force between the opposing interfaces. The Casimir free energy, $F_C(l)$, is therefore normalized to $F = 0$ in the limit $l \rightarrow \infty$. We have

$$F_C(l) = F(l, l_0) - \lim_{l \rightarrow \infty} F(l, l_0) |_{l+l_0=\text{constant}}, \quad (39)$$

where

$$F(l, l_0) = -k_B T \sum_k \ln \left(\Theta_k^{(s)}(l, l_0) \right), \quad (40)$$

and $\Theta_k^{(s)}(l, l_0)$ is defined in Equation (31). It is understood that the total volume of the system is held fixed by imposing $l + l_0 = \text{constant}$, and that l_0 is large compared with any system-specific length scale.

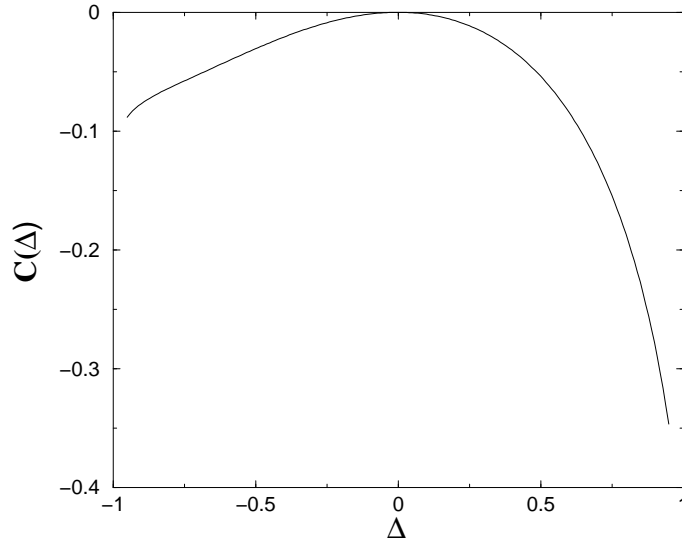


FIG. 3: The function $C(\Delta)$ defined in Equation (44), where $\Delta = (\kappa - \kappa_0)/(\kappa + \kappa_0)$. Note that $C(\Delta) \neq C(-\Delta)$.

A. $\mathbf{m}_0 = \mathbf{m} = \mathbf{0}$

This case corresponds to an untethered membrane which is tensionless, as is the case for a membrane in the presence of the various lipid species in solution. Upon a change in the physical area of the membrane, A , lipid molecules can leave or enter meaning that any area change costs no free energy.

Then we have $\mu_0 = \mu = 0$. In this case, the choice for the general solution to the classical equations of motion is not given by Equation (19) but by

$$X(t) = a \cosh(pt) + b \sinh(pt) + c t \cosh(pt) + d t \sinh(pt) . \quad (41)$$

The method follows the manipulations of section III, and appendix A. We find that

$$F_C(l, \Delta) = \frac{k_B T}{2} \sum_k \ln \left(1 + a_2(l, \Delta) e^{-2kl} + a_4(l, \Delta) e^{-4kl} \right) , \quad (42)$$

where

$$\begin{aligned} a_2(l, \Delta) &= \frac{\Delta^2}{(1 - \Delta^2/4)} \left[k^2 l^2 \left(\frac{1 - \Delta/2}{1 + \Delta/2} \right) - \frac{3}{2} \right] , \\ a_4(l, \Delta) &= \frac{9\Delta^4}{16(1 - \Delta^2/4)^2} . \end{aligned} \quad (43)$$

We note that all terms are invariant under $\Delta \rightarrow -\Delta$ except the first term in $a_2(l)$, and hence the Casimir free energy is not invariant under this transformation in this case. On dimensional grounds we have

$$F_C(l, \Delta) = \frac{C(\Delta) k_B T}{l} , \quad (44)$$

and $C(\Delta)$ is shown in Figure 3. Since $C(\Delta) < 0$ for $\Delta \neq 0$, the Casimir force is attractive and is given by

$$f_C(l, \Delta) = - \frac{\partial}{\partial l} \frac{C(\Delta) k_B T}{l} = \frac{C(\Delta) k_B T}{l^2} , \quad (45)$$

with $|C(\Delta)| \lesssim 0.4$.

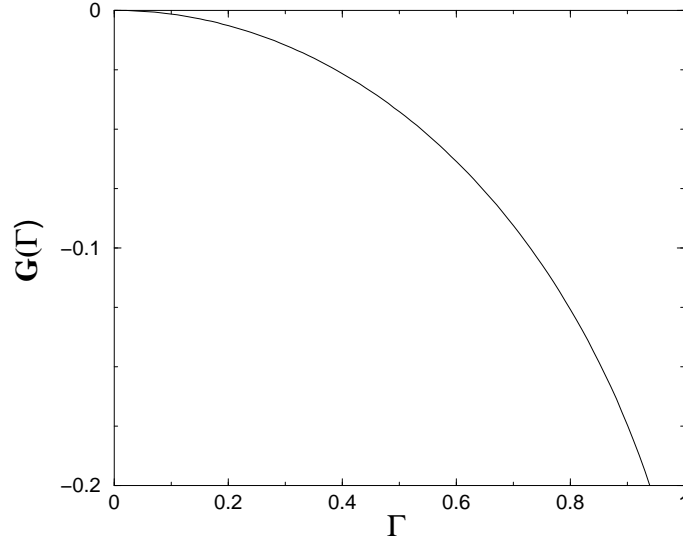


FIG. 4: The function $G(\Gamma)$ defined in Equation (48), where $\Gamma = (\mu - \mu_0)/(\mu + \mu_0)$. Note that $G(\Gamma) = G(-\Gamma)$.

B. $m_0, m > 0$

This case is for non-zero μ_0 and μ . The projected area is constant but any change in the area results in a free energy change. In practice, the typical observed values of μ give $ma \sim 0.3$ (see section III) and consequently the width of the stripe, l , satisfies $l \ll 1/m$. As shown in section III the free energy has a contribution that corresponds to the energy of the interfaces between the stripe and the bulk medium and includes the UV divergent part of the sum over modes. The remaining, l -dependent, terms are UV convergent and are cut-off but exponential factors on a scale $k \lesssim 1/l$. Thus, the Casimir free energy excluding the interface energy gets contributions only from low mode number $k \ll 1/m$ and so we can approximate the eigenvalues in Equations (20) and (21) by

$$p = k, \quad q = m. \quad (46)$$

Also, only leading terms in e^{ql} will survive; the others will be suppressed by factors of e^{-ml} . Following the derivation of the previous subsection, we find a result that is independent of κ_0 and κ , as one might expect on dimensional grounds for $\mu \gg \kappa/l^2$. We get

$$F_G(l, \Gamma) = \frac{k_B T}{2} \sum_k \ln(1 - \Gamma^2 e^{-2kl}), \quad (47)$$

where $\Gamma = (\mu - \mu_0)/(\mu + \mu_0)$. The leading corrections are suppressed by the factor $(1/ml)^2$. For the values of m considered this is of order $(a/l)^2 \sim 1/N^2$, where N is the number of lipid molecules across the strip. Similarly to before we may write

$$F_G(l, \Gamma) = \frac{G(\Gamma)k_B T}{l} + O\left(\frac{1}{(ml)^2}\right). \quad (48)$$

$G(\Gamma)$ is symmetric under $\Gamma \rightarrow -\Gamma$, and is shown in Figure 4. We see that $|G(\Gamma)| \lesssim 0.2$ and, being negative for $\Gamma \neq 0$, gives rise to an attractive Casimir force of maximum magnitude $0.2k_B T/l^2$.

The more general case where $m \sim 1/l$ is very much more complicated and the expressions cannot be presented here but need to be investigated computationally in the three parameter μ, κ, l space. We have verified that this analysis is feasible but complicated and so we have chosen not to present it in this paper. However, any more general result for the Casimir force will interpolate between the two extremes presented here and so we would expect a leading contribution to behave like $-ck_B T/l^2$ with $c \lesssim 1$.

V. CONCLUSION

In this paper we have shown how the formalism developed in earlier work [9] can be applied to the more general case of higher derivative Gaussian energy functions such as apply to the path integral analysis of stiff polymers and the Helfrich model for membranes. Some aspects of this approach have been previously described in the literature [4, 5, 6]. However, our approach is slightly different and self-contained. Hence, for the sake of completeness (and because the results seem to be relatively unknown) we have included a detailed description of this approach. In particular, we have shown how to generalize the Pauli-van Vleck formula for the evolution kernel of all theories of this type.

As a model system we have considered a toroidal lipid membrane with one very large circumference and the other finite of length L , with a stripe of width l wrapped around the finite circumference and of different, minority, lipid type to the bulk, majority, type. This is shown schematically in Figure 1. This geometry imposes periodic boundary conditions on the system. We have shown how to compute, in general, two important energies in this system, namely the energy, or line tension, associated with the lipid-lipid interface and the Casimir force between the interfaces, as a function of width l . An important controlling parameter, m , has the dimensions of a mass and is given by $m^2 = \mu/\kappa$. We have presented these calculations explicitly for the cases where $m = 0$ and $ma \sim 1$, $l \gg 1/m$, where a is the inter-lipid spacing. These correspond, respectively, to the cases where the actual area, A , or the projected area, A_p , is conserved. In the latter case, we calculate the mean excess area of the system $\Delta A/A_p$ in section III. In both cases, the interface energy is positive and the Casimir force attractive as can be seen from Equations (35), (44), (48) and the associated figures. Our general result is that in appropriate dimensionful units the energy coefficient is $ck_B T$ where, at maximum, $c \sim 1$. This is to be compared with the natural bending rigidity which lies in the range $5k_B T \leq \kappa \leq 100k_B T$.

The general case where $l \sim 1/m$ is complicated and long, and although we have the results we have not presented an explicit analysis in the μ, κ, l parameter space because of the complexity. However, there is no computational or algebraic impediment to carrying this out.

In terms of relevance to the physical system we might consider two scenarios in the two-lipid model discussed here. Either the minority lipid can be dissolved in the majority lipid to form a homogeneous phase for the mixture, or the minority lipid can precipitate out of solution and form a pure minority phase, the stripe in our idealized case, within the pure majority phase. Which situation is stable is, of course, decided by a competition between the free energies of the configurations which is in turn dependent on the boundary conditions imposed. However, it is clear that the attractive Casimir force will tend to reduce the stripe width l , presumably by evaporation of minority lipid from the interface into solution. The interface energy is constant throughout such a process but will always tend to minimize the interface length. A stability analysis, however, requires a computation of the free energy of the mixed phase which our calculation does not address. However, as has been discussed in [16], the suppression of lipid mode fluctuations by confining the membrane in a stack will change the free-energy of both configurations and so can affect their stability; an effect which can be analyzed by our methods.

APPENDIX A: THE GENERALIZED PAULI-VAN VLECK FORMULA

In this appendix we show how generalized quadratic path integrals can be evaluated giving a generalization of the Pauli-van Vleck formula. The treatment is very close to that of [6] and is based on the Chapman-Kolmogorov decomposition of the path integral. We consider the following path integral

$$K(\mathbf{X}, \mathbf{Y}; t) = \int_{\mathbf{X}(0)=\mathbf{X}}^{\mathbf{X}(t)=\mathbf{Y}} d[X] \exp(-S[X]), \quad (\text{A1})$$

where S is a quadratic action which will have the general form

$$S[X] = \frac{1}{2} \int_0^t ds \sum_{k=0}^N a_k \left(\frac{d^k X}{ds^k} \right)^2. \quad (\text{A2})$$

In general the coefficients a_k can be time dependent but for the problems related to membranes studied here we will only require the results for a_k constant. The usual Wiener measure occurring in path integrals has $N = 1$ and the corresponding path integral is that for standard Brownian motion, or a free particle, with $a_0 = 0$. If $a_0 \neq 0$ in this case, then the path integral corresponds to that of a simple harmonic oscillator with $a_0 = m\omega^2$ and $a_1 = m$ thus relating the coefficients a_i , $i = 0, 1$ to the mass m and frequency of the oscillator. The path integrals arising in section II are, of course, for the case $N = 2$ which, as mentioned above, also arises for the path integrals of stiff or semi-flexible polymers. We also refer the reader to the approach of [4] which is based on an eigenfunction expansion method for the case $N = 2$.

Now one must state how the initial and final points of the path integral should be specified. The presence of the term $(d^N X/ds^N)^2$ means that the paths that contribute to the path integral are ones where the derivatives $d^{N-1}X/ds^{N-1}$ and lower must be continuous. The path integral should therefore be specified in terms of the vector $\mathbf{X} = (X, X^{(1)}, X^{(2)} \dots X^{(N-1)})$ where we have used the notation $X^{(k)} = d^k X/ds^k$. We can now decompose the path integral using the Chapman-Kolmogorov formula

$$K(\mathbf{X}, \mathbf{Z}; t + t') = \int d\mathbf{Y} K(\mathbf{X}, \mathbf{Y}; t) K(\mathbf{Y}, \mathbf{Z}; t'). \quad (\text{A3})$$

This decomposition ensures the continuity of the path $X(t)$ up to its $N - 1$ th derivative.

The classical path is given by the one that minimizes the action:

$$\frac{\delta S}{\delta X(s)} = 0, \quad (\text{A4})$$

with the boundary conditions on the end points $\mathbf{X}(0) = \mathbf{X}$ and $\mathbf{X}(t) = \mathbf{Y}$. This gives a total of $2N$ boundary conditions (N from each end). The equation for the classical path can be written as

$$\int ds' \frac{\delta^2 S}{\delta X(s) \delta X(s')} X_{cl}(s') = 0, \quad (\text{A5})$$

which is a linear differential equation of order $2N$. For instance, when the a_k are constant it reads

$$\sum_{k=0}^N (-1)^k a_k \frac{d^{2k}}{dt^{2k}} X_{cl}(s) = 0. \quad (\text{A6})$$

There are thus $2N$ linearly independent solutions to this equation and their coefficients are linearly related to the $2N$ conditions for the end points. The classical action is a quadratic form in the initial and final condition vectors \mathbf{X} and \mathbf{Y} and we can write

$$S_{cl}(\mathbf{X}, \mathbf{Y}) = \frac{1}{2} [\mathbf{X}^T A_I(t) \mathbf{X} + \mathbf{Y}^T A_F(t) \mathbf{Y} - 2\mathbf{X}^T B(t) \mathbf{Y}], \quad (\text{A7})$$

where we have used the subscripts I and F to denote the initial and final coordinates. We now write the path $X(s)$ as $X(s) = X_{cl}(s) + x(s)$, where the boundary conditions imply that $\mathbf{x}(0) = \mathbf{0}$ and $\mathbf{x}(t) = \mathbf{0}$. The path integral can now be written as

$$\begin{aligned} K(\mathbf{X}, \mathbf{Y}; t) &= \exp(-S_{cl}(\mathbf{X}, \mathbf{Y})) \int_0^0 d[x] \exp\left(-\frac{1}{2} \int_0^t ds ds' x(s') \frac{\delta^2 S}{\delta X(s) \delta X(s')} x(s)\right) \\ &= Q(t) \exp(-S_{cl}(\mathbf{X}, \mathbf{Y})), \end{aligned} \quad (\text{A8})$$

where we formally write can write

$$Q(t) = \det\left(\frac{\delta^2 S}{\delta X(s) \delta X(s')}\right)^{-\frac{1}{2}}, \quad 0 \leq s, s' \leq t. \quad (\text{A9})$$

The above functional determinant can be evaluated using an eigenfunction expansion, however for higher order operators this quickly becomes impractical. Instead, we return to the Chapman Kolmogorov formula Equation (A3) and pursue its consequences using the formal result Equation (A8). Explicitly carrying out the intermediate integration over \mathbf{Z} , we find that

$$\begin{aligned} K(\mathbf{X}, \mathbf{Z}; t + t') &= (2\pi)^{\frac{N}{2}} Q(t) Q(t') \det(A_I(t) + A_F(t'))^{-\frac{1}{2}} \times \\ &\quad \exp\left(-\frac{1}{2} \mathbf{X}^T [A_I(t) - B(t)(A_I(t') + A_F(t))^{-1} B^T(t)] \mathbf{X}\right) \times \\ &\quad \exp\left(-\frac{1}{2} \mathbf{Z}^T [A_F(t') - B^T(t')(A_I(t') + A_F(t))^{-1} B(t)] \mathbf{Z}\right) \times \\ &\quad \exp(\mathbf{X}^T B(t)(A_I(t') + A_F(t))^{-1} B^T(t') \mathbf{Z}), \end{aligned} \quad (\text{A10})$$

Now comparing the quadratic forms and prefactors we find the following relations:

$$A_I(t+t') = A_I(t) - B(t)(A_I(t') + A_F(t))^{-1}B^T(t) \quad (\text{A11})$$

$$A_F(t+t') = A_F(t') - B^T(t')(A_I(t') + A_F(t))^{-1}B(t') \quad (\text{A12})$$

$$B(t+t') = B(t)(A_I(t') + A_F(t))^{-1}B(t') \quad (\text{A13})$$

$$Q(t+t') = (2\pi)^{\frac{N}{2}}Q(t)Q(t')\det(A_I(t) + A_F(t'))^{-\frac{1}{2}}. \quad (\text{A14})$$

In [6] it is pointed out that relation Equation (A14) above can be used to derive a differential equation for Q . However, a more rapid way of finding Q is to note that taking the determinant of both sides of Equation (A13) gives

$$\det(B(t+t')) = \det(B(t))\det(B(t'))\det(A_I(t) + A_F(t'))^{-1}, \quad (\text{A15})$$

and using this relation we find that by direct substitution into Equation (A14) that the solution for Q is

$$Q(t) = (2\pi)^{-\frac{N}{2}} [\det(B(t))]^{\frac{1}{2}}. \quad (\text{A16})$$

The generalized form of the Pauli-van Vleck formula may thus be written in the familiar form (for $N = 1$ and its generalization to higher dimensions)

$$K(\mathbf{X}, \mathbf{Y}; t) = (2\pi)^{-\frac{N}{2}} \det \left[\frac{\partial S_{cl}}{\partial X_i \partial Y_j} \right]^{\frac{1}{2}} \exp(-S_{cl}(\mathbf{X}, \mathbf{Y})). \quad (\text{A17})$$

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